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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/822,110	03/30/2001	Hwa-Chain Robert Wang	4350.000800	9178

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WILLIAMS, MORGAN & AMERSON, P.C.
10333 RICHMOND, SUITE 1100
HOUSTON, TX 77042

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/822,110	WANG, HWA-CHAIN ROBERT	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,12,42-52,61-63 and 76-83* is/are pending in the application.

4a) Of the above claim(s) *76-83* is/are withdrawn from consideration.

5)☒ Claim(s) *9,12 and 61-63* is/are allowed.

6)☒ Claim(s) *1-7 and 49* is/are rejected.

7)☒ Claim(s) *42-48 and 50-52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 08/03/04 is acknowledged.

Claims 1-7, 9, 12, 42-52, 61-63 and 76-83 are pending.

Newly submitted claims 76-83 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The elected Group III, claims 1-7,9, 12, 42-52 and 61-63 drawn to an isolated mammalian peptide. Newly submitted claims 76-83 drawn to a fusion polypeptide. These invention are patentably distinct product because they differ with respect to their structures and physicochemical properties, and have a separate status in the art as shown by their different classification which require non-coextensive searches.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 76-83 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-7, 9, 12, 42-52, 61-63 are under consideration in the instant application.

2. Claims 42-52 are objected to under 37 CFR § 1.75(c) as being improper multiple dependent claims because base claims 9 and 12 recite two different features.

3. In view of the amendment, filed 08/03/04 the following rejections remain.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-7 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record set forth in the Office Action, filed 01/30/04.

Applicant's arguments, filed 11/03/03 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) the terms "about" serves reasonably to define the claimed invention ; (ii) in several issued US Patents the term "about" have been used to describe the approximate length of amino acid sequence.

Contrary to Applicant's assertions, the use of term "about" in the instant application refers to the number of amino acid of SEQ ID NOs: 3-76 which does render the claims indefinite. It is unclear how many amino acids constitute "about" or 'approximately". One of skill in the art would not know if applicant meant 14 amino acid or as many as 70 amino acids, or even more and this is critical for the claimed inventions.

With regards to Applicant's assertion that in several issued US Patents the term "about" have been used to describe the approximate length of amino acid sequence.

It is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991). Moreover, as stated In re Borkowski, 505 F2d 713,718,184 USPQ29,33 (CCPA 1974), "The Paten Office must have the flexibility to reconside and correct prior decisions that may find to have been in error". In a similar context, the court in Fessenden v.Coe, 38 USPQ 516,521 (CADC 1938) stated that '[t]wo wrongs cannot make a right."

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 2 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

"An isolated peptide consisting essentially of the amino acid sequence of any one of SEQ ID NOs...." claimed in Claim 2 represent(s) a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come(s) from. The specification and the claims as originally field only support "An isolated peptide comprising of the amino acid sequence of any one of SEQ ID NOs...."

8. Claims 1-7 and 49 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO: 2, a peptide consisting of residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76, said SEQ ID NO: 2/peptides in a pharmaceutically acceptable excipient and a kit comprising said peptides, does not reasonably provide enablement for any isolated peptide/polypeptide from 16 to about20/30/40/50/60/70 amino acids in length comprising or consisting essentially any one of SEQ ID NOS: 3-76. or a composition wherein one detection reagent specifically binds to peptide or antibody, as recited in claim 49. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons of record set forth in the Office Action, filed on 01/30/04.

Applicant's arguments, filed 11/03/03 have been fully considered, but have not been found convincing.

Applicant asserts that Specification clearly satisfies the "make and use" requirement of the statute, by providing several examples of peptides and polypeptides that comprise one or more amino acid sequence disclosed in the Specification.

Contrary to Applicants assertion, the claims as written encompass the genus of peptide and polypeptide amino acid sequences. The genus encompasses peptides wherein such peptides have numerous differences in amino acid sequences.

Applicant discloses a single polypeptide comprising SEQ ID NO: 2 (491 residues), a peptide consisting of amino acid residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76 in the instant specification. Applicant has taught a polypeptide comprising SEQ ID NO: 2, peptides consisting of SEQ ID NOS: 3-76 and a peptide consisting of amino acid residues 1-322 of SEQ ID NO: 2. Applicant has not taught how to make and/or use any isolated peptide from 14 to about 20/30/40/50/60/70 amino acids in length other than peptides consisting of SEQ ID NOS: 3-76. The structural and functional characteristics of said peptides are not defined in the claim.

Also the issue that it is unclear how a detection reagent comprising a spin label, a radiolabel, a fluorogenic label, a chromogenic label, a chemiluminescent label, can specifically binds to a polypeptide or antibody, as recited in claim 49. It was well known in the art at the time the invention was made that said detectable label are linked or attached to polypeptide or peptide or antibody thus providing the means for detection said products.

"Comprising" and "consisting essentially" are considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a peptide "comprising" or "consisting essentially" from 14 to about 20/30/40/50/60/70 amino acids in length of SEQ ID NOS: 3-76 includes an unlimited number of amino acid sequences "comprising" or "consisting

essentially" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 3-76 cannot support the entire genus of peptides from 14 to about 20/30/40/50/60/70 as part of their sequence.

It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular).

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated amino acids from 14 to about 20/30/40/50/60/70 amino acids in length having "SEQ ID NOS: 3-76 encompassed by the claimed invention other than "amino acids set forth by SEQ ID NO: 2" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. generation of antibodies which recognize p33) requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain functional aspects the peptides and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation.

In re Fisher, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and

492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention.

However, the present specification fails to provide sufficient disclosure of such polypeptides that maintain the structural and functional properties of the p33 polypeptide set forth in SEQ ID NO: 2 wherein the other amino acids can vary. The specification does not provide sufficient guidance as to which of the amino acids may be changed while p33 polypeptide/peptide structural or functional activity and specificity is retained. Further, the specification fails to provide guidance as to the unlimited number of polypeptides which can be fusion partners for peptides comprising from 16 to about 70 amino acids in length of SEQ ID NOS: 3-76 and residues 1-322 of SEQ ID NO: 2.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed any isolated peptide/polypeptide from 16 to about20/30/40/50/60/70 amino acids in length comprising or consisting essentially any one of SEQ ID NOS: 3-76. or a composition wherein one detection reagent specifically binds to peptide or antibody, as recited in claim 49 in manner reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by the genus of polypeptides as recited in the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 1-7 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record set forth in the Office Action, filed on 09/30/02.

Applicant's arguments, filed 11/03/03 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) Specification on pages 5 to 17 provides "an exhaustive and detailed teaching" that describes how to make and use various polypeptides or peptides and that Specification clearly indicates that "one aspect of the invention involves composition that comprises at least a first isolated peptide of from 9 to about 80 amino acids in length or at least first nucleic acid segment that encodes such a peptide, wherein the peptide comprises, consists

essentially of a first contiguous animo acid sequence according to any one of SEQ ID NOs 3 – 76."; (ii) the amended claims now recited a specific functional characteristic i.e. binding to Krs-1-NC antibody.

Contrary to Applicant's assertion, as was stated in the Office Action, filed on 09/30/02. it was stated:

"Conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). A description of a genus of polypeptide/peptide sequences may be achieved by means of a recitation of a representative number of polypeptides/peptides having SEQ ID NOS: 3-76, residues 1-322 of SEQ ID NO: 2, or at least a first peptide and at least a second peptide of SEQ ID NOS: 3-76, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)".

Moreover, the ability of a peptide to bind to to Krs-1-NC antibodyis not a specific functional property , because an antibody epitope may be as small as 6-15 shared amino acid residues and places no limitations on the function of the protein containing the polypeptide sequence recognized. In addition, a description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

Applicant is in possession of a polypeptide comprising SEQ ID NO: 2, a peptide consisting of residues 1-322 of SEQ ID NO: 2, and peptides consisting of SEQ ID NOS: 3-76, said SEQ ID NO: 2/peptides in a pharmaceutically acceptable excipient and a kit comprising said peptides.

Applicant is not in possession any isolated peptide/polypeptide from 16 to about20/30/40/50/60/70 amino acids in length comprising or consisting essentially any one of SEQ ID NOS: 3-76. or a composition wherein one detection reagent specifically binds to peptide or antibody, as recited in claim 49.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001.

The following new ground of rejection is necessitated by amendment filed 08/03/04

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

12. In claims 1-7 , it is apparent that the Krs1-NC antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

If the deposit have been made under the terms of the Budapest treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the

hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806 1.808 (a)(2) and MPEP 2410-2410.01.

If the deposit has not been made under the Budapest treaty, then an affidevit or declaration by Applicants or someone associated with the patent owner who is in position to make such assurances, or statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of the deposit and complete name and address of the depository is required.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

13. Claims 9, 12, and 61-63 are allowable.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
September 7, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600